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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/819,104	03/27/2001	J. Don Chen	UMG-030	4327

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EXAMINER	
MURPHY, JOSEPH F	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 02/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/819,104	CHEN, J. DON	
	Examiner	Art Unit	
	Joseph F Murphy	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *1-18 and 27-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a)☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2/27/2003* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence Comparison A.*

DETAILED ACTION

Election/Restrictions

Applicant's election of Group XI, claims 19-26 in the Paper submitted 10/22/2003 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 1-29 are pending. Claims 1-18, 27-29 are withdrawn from consideration pursuant to 37 CFR 1.142(b). Claims 19-26 are under consideration.

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. Applicant should restrict the title to the claimed invention.

Applicant should avoid the use of novel in the title, as patents are presumed to be novel and unobvious.

Information Disclosure Statement

References A1 and A2 on the IDS of 2/27/2003 have been lined through because they are not in the correct format. The citation should include the author and publication date, pursuant to 37 CFR 1.98.

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, which is enabling for a method for identifying a compound which binds to a polypeptide with the sequence as set forth in SEQ ID NO: 2, does not reasonably provide enablement for methods of identification of compounds that bind to as polypeptide which is selected from the group consisting of fragments of a polypeptide of SEQ ID NO: 2, or polypeptides encoded by nucleic acids which hybridize to SEQ ID NO: 1, or polypeptides encoded by nucleic acids having 50% homology to SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The claims are drawn to methods of identification of compounds that bind to as polypeptide as set forth in non-elected claim 8. Claim 8 is drawn to a polypeptide which is selected from fragments of a polypeptide of SEQ ID NO: 2, or polypeptides encoded by nucleic acids which hybridize to SEQ ID NO: 1, or polypeptides encoded by nucleic acids having 50% homology to SEQ ID NO: 1. Since the claims are thus directed to methods using variant polypeptides and Applicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible muteins of SMRTe, Claims 19-26 are overly broad since insufficient guidance is provided as to which of the myriad of variant polypeptides encompassed by the claimed methods will retain the function or characteristics of a SMRTe

polypeptide. It is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. As an example of the unpredictable effects of mutations on protein function, Mickle et al. teaches that cystic fibrosis is an autosomal recessive disorder caused by abnormal function of a chloride channel, referred to as the cystic fibrosis transmembrane conductance regulator (CFTR) (page 597). Several mutations can cause CF, including the G551D mutation. In this mutation a glycine replaces the aspartic acid at position 551, giving rise to the CF phenotype. In the most common CF mutation, delta-F508, a single phenylalanine is deleted at position 508, giving ride to the CF phenotype. Thus showing that even the substitution or deletion of a single amino acid in the entire 1480 amino acid CFTR protein sequence can have dramatic and unpredictable effects on the function of the protein. Additionally, it is known in the art that even a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. For example, Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph). Since the claims encompass methods using variant polypeptides and given the art recognized unpredictability of the effect of mutations on protein function, it would require undue experimentation to make and use the claimed invention. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The amino acid sequence of a

polypeptide determines its structural and functional properties, and the predictability of which amino acids can be substituted is extremely complex and outside the realm of routine experimentation, because accurate predictions of a polypeptide's structure from mere sequence data are limited. Since detailed information regarding the structural and functional requirements of the polynucleotide and the encoded polypeptide are lacking, it is unpredictable as to which variations, if any, meet the limitations of the claims. Applicant is required to enable one of skill in the art to make and use the claimed invention, while the claims encompass methods using encoded polypeptides that the specification only teaches one skilled in the art to test for functional variants. It would require undue experimentation for one of skill in the art to practice the claimed methods using the encompassed polypeptides. Applicant is required to enable one of skill in the art to make and use the claimed invention, while the claims encompass polypeptides that the specification only teaches one skilled in the art to test for functional variants. Since the claims do not enable one of skill in the art to make and use the claimed polypeptides, but only teaches how to screen for the claimed polypeptides, and since detailed information regarding the structural and functional requirements of the polypeptides are lacking, it is unpredictable as to which variations, if any, meet the limitations of the claims. Thus, since Applicant has only taught how to test for polypeptide variants of SMRTe, and has not taught how to make polypeptide variants of SMRTe, it would require undue experimentation of one of skill in the art to practice the claimed methods.

Claims 19-26 are rejected, under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The claims are drawn to methods of identification of compounds that bind to as polypeptide as set forth in non-elected claim 8. Claim 8 is drawn to methods using a polypeptide which is selected from fragments of a polypeptide of SEQ ID NO: 2, or polypeptides encoded by nucleic acids which hybridize to SEQ ID NO: 1, or polypeptides encoded by nucleic acids having 50% homology to SEQ ID NO: 1, thus these are genus claims. The claims are directed to methods utilizing variant polypeptides. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. The specification and claims do not place any limit on the number of amino acid substitutions, deletions, insertions and/or additions that may be made to the SMRTe variants. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claim do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the

common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO: 2 is insufficient to describe the genus. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. In the instant case, the specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the genus of polypeptides. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from other seven transmembrane region compounds are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polynucleotides and polypeptides encompassed. Thus, no identifying characteristics or properties of the instant polypeptides are provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

In addition, due to the limitation of "allelic variant" recited in claim 8, from which claims 19-26 depend, a determination of what the claim as a whole covers indicates that elements which are not particularly described, e.g. the sequence of the claimed allelic variants, are encompassed by this claim. There is no actual reduction to practice of the claimed invention, or complete detailed description of the structure. A biomolecular sequence described only by a functional characteristic, in this case an allelic variant of a protein whose sequence is set forth in SEQ ID NO: 2, without any known or disclosed correlation between the function and the structure of the sequence is not a sufficient identifying characteristic. See University of California v. Eli Lilly and Co. 43 USPQ2d at 1406. There is no known or disclosed correlation between this function and the structure of the non-described allelic variants and the disclosed polypeptide with an amino acid sequence as set forth in SEQ ID NO: 2. Weighing all factors in view of the level of knowledge and skill in the art, one skilled in the art would not recognize from the disclosure that the Applicant was in possession of the claimed invention.

Claim Rejections - 35 USC § 112 second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 19-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are drawn to methods of identification of compounds that bind to as polypeptide as set forth in non-elected claim 8. Claim 8 is drawn to polypeptides encoded by nucleic acids that hybridize to SEQ ID NO: 1 under "stringent conditions". This is a conditional

term and renders the claim indefinite. Furthermore, some nucleic acids which might hybridize under conditions of moderate stringency, for example, would fail to hybridize under conditions of high stringency. The metes and bounds of the claim thus cannot be ascertained. This rejection could be obviated by supplying specific conditions supported by the specification which Applicant considers to be "stringent". Claims 19-26 are rejected insofar as they depend on the recitation in claim 8 of "stringent conditions".

Claim 8 recites the term "naturally occurring". It is unclear whether this term imposes a required limitation on the claim, such that it only encompasses, for example, polypeptides isolated from tissue expressing the polypeptide, or only sequences produced by translation from DNA isolated from tissue which contains polynucleotides encoding the polypeptide, or if the claim encompasses all polypeptide sequences. Therefore, the metes and bounds of the claim are unclear. Claims 19-26 are rejected insofar as they depend on the recitation in claim 8 of "naturally occurring".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 19-26 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 97/09418 (Evans et al.).

The claims are drawn to methods of identification of compounds that bind to as polypeptide as set forth in non-elected claim 8. Claim 8 is drawn to polypeptides which is selected from fragments of a polypeptide of SEQ ID NO: 2, or polypeptides encoded by nucleic acids which hybridize to SEQ ID NO: 1, or polypeptides encoded by nucleic acids having 50% homology to SEQ ID NO: 1. The Evans reference teaches a nuclear co repressor which interacts with the retinoic acid receptor (page 2, lines 20-29). The amino acid sequence of the SMRT polypeptide is 57.5% identical to the polypeptide of claim 8, and comprises sequence fragments identical to SEQ ID NO: 2 which are more than 15 amino acids in length (see Sequence Comparison A, attached). The Evans reference also teaches methods of identifying compounds that bind to the SMRT protein (page 7, line 34 to page 9, line 27). Since the instant claims are drawn to methods utilizing the polypeptide of claim 8, and claim 8 encompasses the polypeptide as taught in the Evans reference, which also teaches methods of identifying compounds using the protein, the claims are anticipated.

Conclusion

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
January 8, 2004